Dose-response analysis of aripiprazole in Taiwanese schizophrenic patients

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Background To optimize the efficacy and further decrease the long-term discontinuation, the dose-response analysis of antipsychotic drugs is important. Previous research determined the therapeutic serum concentration of aripiprazole with heterogeneous results ranging from 100 to 350 ng/ml. (1,2) And the curve of dose-response of aripiprazole was slightly bell-shaped which indicated the effectiveness was not always associated with higher doses.(3) There's still a lack of information on predicted factors that help clinical psychiatrists determine the target dose of aripiprazole in each patient individually.

Aims & Objectives To analyze the dose-response relationship and associated factors of aripiprazole in the Chinese schizophrenic population.

Methods Patients with a diagnosis of schizophrenia from the outpatient department or acute psychiatric inpatient ward between 1 January 2017 to 1 June 2018 were considered for inclusion in this study. Dose and type of other psychotropic agents remained consistent during the data collection of this study. The blood samples were taken after the daily dose of aripiprazole remained consistent for more than 28 days. After dose modification was accomplished, effectiveness measures included the CGI response rate, which is defined as a CGI score 2 compared with the first assessment time point.

Results The mean concentration of aripiprazole was 432.1±275.1 ng/ml in the study cohort. Among patients with at least a much-improved according to the CGI-I scores, mean serum concentration of aripiprazole was 494±273 ng/ml (25th –75th percentiles 264–666 ng/ml) and were higher than the current recommended therapeutic target of 100–350 ng/ml for aripiprazole. The response rate in the severe group (baseline CGI score of 6 and 7) was significantly higher than in the moderate group (baseline CGI score of 4 and 5) (86.7% vs. 55.9%, p=0.007, respectively). Higher, but not significant, compliance represented by dose-corrected serum concentration were found in inpatients (26.6±4.0 ng/ml/mg) compared with outpatients (19.4±9.8 ng/ml/mg) (p=0.068).

Discussion & Conclusion In patients with schizophrenia, therapeutic nonadherence due to poor insight, psychotic symptoms, and adverse effects would lead to poorer prognosis and quality of life. (4,5) Though there was no significant difference of drug adherence between inpatients and outpatients in our study population, therapeutic drug monitoring still plays an important role in clinical practice. Therapeutic drug monitoring is recommended in some circumstances, for instance, to optimize the clinical response and to reduce possible toxicity. (5,6) Previous review articles of the dose-response relationship of aripiprazole in schizophrenia and schizoaffective disorder pointed out that there's no additional benefit for doses above 20mg/d. (7) But we found that in participants showing at least a much-improved level according to the CGI-I scale, aripiprazole serum levels were much higher than the recommended therapeutic serum concentration. If clinically indicated and the patient was tolerable, a higher daily dose of aripiprazole may potentially lead to better efficacy and greater improvement